Mesenchymal Stem Cell Extracellular Vesicles for Inflammatory Bowel Disease

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Inflammatory bowel disease (IBD) is a chronic and progressive disorder, characterised by destructive inflammation of small and/or large intestine. The prevalence of this disorder is increasing globally (from 79.5 per 100,000 population in 1990 to 84.3 per 100,000 population in 2017), with around 6.8 million cases worldwide in 2017 [1]. Healing of the inflamed mucosa is an emerging and important therapeutic goal in IBD. Mucosal healing and re-establishment of the intestinal barrier are associated with clinical remission and improved patient outcomes. Currently, however, this is not achieved effectively with conventional treatments, including biologics, resulting in a need for surgery. Therefore, novel treatment strategies that achieve intestinal mucosa healing and re-establishment of normal barrier integrity are urgently required.

(Small) extracellular vesicles (EVs) are 30–150 nm lipid bilayer membrane vesicles released from most living cells into the extracellular medium and function as cell communication shuttles with intercellular signalling capabilities. They carry proteins, mRNAs, microRNA, DNA and lipids between cells. EVs produced from mesenchymal stem cells (MSCs) have significant tissue regenerative and anti-inflammatory properties. Stem cell EVs, which have been described as the 'secret sauce' of stem cells, therefore have tremendous therapeutic potential. In this work, we investigated the therapeutic potential of orally administered MSC EVs in IBD.

EVs were isolated using ultracentrifugation and characterised for expression of common exosomal proteins, as well as size (nanoparticle tracking analysis, dynamic light scattering), charge (zeta potential) and morphology (electron microscopy). EVs were tested in fed-state and fasted-state simulated intestinal fluids. EVs were also coated and the effect of this coating on gut stability tested. The therapeutic potential of MSC EVs was tested in a novel in vitro cell co-culture model and in an animal model of IBD. These systems showed anti-inflammatory properties and reduced disease severity in an IBD animal model, highlighting that MSC EVs demonstrate potential as oral therapies for IBD.

References

[1] Ng et al, Lancet, 390 (2017). 2769-2778